REMARKS

Claims 1-17 are pending in the application. Applicants have amended claims 1, 11, and 13. Claim 12 has been canceled.

Upon entry of the present amendment, claims 1-11 and 13-17 remain pending in this application.

Claims 1-17 stand rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. Specifically, the recitation of the limitations of $(C_1\text{-}C_6)$alkyl was thought to be unclear.

According to the second square bullet, R^2 may indeed be $(C_1\text{-}C_6)$alkyl substituted with $OC(=O)R^{4a}$, $NR\text{-}SO_2\text{-}R^3$, $RN\text{-}SO_2\text{-}NR^{4a}R^{5a}$ or $NR\text{-}CO\text{-}NR^{4a}R^{5a}$.

According to the first square bullet, R^2 may also be $(C_1\text{-}C_6)$alkyl substituted with one to three OR^4, $COOR^4$, NR^4R^5, $NRC(=O)R^4$, $C(=O)NR^4R^5$ or $SO_2NR^4R^5$. However, in these definitions, R^4 is $(C_1\text{-}C_6)$alkyl which is further substituted. Therefore, the groups envisaged by the Examiner are, in fact, O-alkyl-$C(=O)R^7$, $N(R^5)$-alkyl-SO_2R^6, $N(R^5)$- alkyl-$SO_2NR^7R^8$ and $N(R^5)$-alkyl-$C(=O)NR^7R^8$. Applicants respectfully submit that these definitions do not overlap with those of the second square bullet.

Claim 11 was specifically rejected as it was allegedly unclear if species were being claimed or a mixture of some (or all) species were being claimed. Applicants have amended claim 11 to overcome this rejection.

Claims 2-10 and 12-17 were rejected as being dependent on claim 1. Applicants have amended claim 1 thereby rendering moot the objection to these claims.

Accordingly, Applicants respectfully submit that all of the rejections to the claims under 35 U.S.C. § 112, second paragraph, have been overcome and reconsideration of the rejections is respectfully requested.

Claims 12-16 stand rejected under 35 U.S.C. § 112, first paragraph, because as stated in the Office Action, the specification, while being enabling for the treatment of AIDS (or HIV infection), allegedly does not reasonably provide enablement for the treatment of other diseases such as: T-cell related diseases, autoimmune diseases, osteoarthritis, rheumatoid arthritis, multiple sclerosis, osteoporosis, chronic obstructive pulmonary disease (COPD), asthma, cancer, leukemia, allergy, inflammatory bowel disease (IBD), ulcerative colitis, Crohn 's disease, pancreatitis, dermatoses, psoriasis, atopic dermatitis, glomerulonephritis, conjunctivitis, autoimmune diabetes, graft rejection, epilepsy, muscular atrophy and systemic lupus erythematosus. It is further alleged in the Office Action that the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with the claims.

At the outset, the Applicants acknowledge and appreciate the Examiner's indication that the treatment of AIDS (or HIV infection) is enabled by the specification. Applicants respectfully submit that the following diseases/conditions are also enabled by the specification: allergy, asthma, T-cell mediated disease, dermatoses (atopic dermatitis), cancer (leukemia), and osteoporosis.

The Applicants respectfully contend that claims 12-16 are enabling with respect to the full scope of the claims; however, in order to advance the prosecution of the present invention Applicants have amended claim 13. Applicants reserve their right to file a divisional application directed to the canceled subject matter in due course.

Upon review and consideration of the rejections set forth in the office action, Applicants contend that the specification enables any person skilled in the art to which the invention pertains, or with which it is most nearly connected, to use the invention commensurate in scope with the amended claim 13.

Applicants respectfully submit that one skilled in the art would find the asserted utility of the claimed compounds consistent with the knowledge in the art at the time of the filing of the application covering the present invention. The scientific literature establishes a direct relationship between PDE7 inhibition and the claimed utilities. To establish this relationship the following literature references are provided below in Table 1, which describes the association between the mechanism of the claimed compounds and the claimed utilities.

Table I

Claimed Disorder	Literature Reference	Disorder in Literature Reference
Allergy and asthma:	Schudt, C. et al, Pulmonary Pharmacology and Therapeutics (1999) **12**, 123-129	This paper provides a potential link between PDE7 and asthma, and presents data in a table (table 2) showing the expression of PDE7 in human cells (including endothelial cells).
	Fuhrmann, M. et al, Am. J. Respir. Cell Mol. Biol. (1999) **20**; 292-302	This paper shows the expression of PDE7 mRNA in human and porcine airway epithelial cells (figures 1-3) but it is difficult to characterise the protein due to the fact that no antibodies or inhibitors were known at the time. But this paper does provide a potential link between PDE7 and airway inflammation (e.g. asthma, COPD).
	Wright, L. et al AJP Lung Cell Mol. Physiol. **275**; L694-L700 (1998)	This paper shows the expression of PDE7 mRNA in human epithelial cells (figure 5) and hence provides a link between PDE7 and airway inflammation.
T-cell mediated disease:	Kanda, N. and Watanabe, S. Biochemical Pharmacology (2001), **62**, 495-507	This paper shows that PDE7 antisense DNA blocks PDE1,2,3,4-independent activity induced by phytohemagglutinin or

Claimed Disorder	Literature Reference	Disorder in Literature Reference
		anti-CD3 plus anti-CD28 in T-cells. Furthermore, PDE7 mRNA is increased in stimulated T cells (stimulated by anti-CD3 plus anti-CD28). The paper therefore provides a link between PDE7 and T-cell mediated disease.
	Li, L. et al Science (1999) 283; 848-851	This paper shows the induction of PDE7 and the consequent suppression of cAMP-dep-PKA activity is required for T-cell activation. Therefore, they postulate that PDE7 inhibitors could be an approach for treating T-cell dependent disorders.
	Nakata, A. et al Clin Exp Immunol. (2002) 128; 460-466	This paper links PDE7 to T-cell mediated diseases (specifically immunological and inflammatory disorders – e.g. asthma, allergic dermatitis) and they show that a PDE7 inhibitor (T-2585) decreases IL-5 synthesis, decreased proliferation and decreased CD25 expression in peripheral blood mononuclear cells (PBMC). (IL-5 is a key inflammatory cytokine.)
Dermatoses – atopic dermatitis:	Gantner, F. et al British Journal of Pharmacology (1998) 123; 1031-1038	This paper shows PDE7 activity and mRNA at high levels in normal B-cells (from non-atopic patients) and in atopic B-cells (patients with atopic dermatitis) (figure 1). This therefore provides a link between PDE7 and dermatoses.

Claimed Disorder	Literature Reference	Disorder in Literature Reference
Cancer – leukaemia:	Lee, R. et al Cellular Signalling (2002 – April) 14 277-284	This paper provides a link between PDE7 and leukemia. They show PDE7 protein expression in normal B-cells, primary chronic lymphocytic leukemia (CLL) cells and in a CLL-derived cell line (WSU-CLL) and PDE7 levels were augmented by treatment of these cells with methylxanthines (non-specific PDE inhibitor).
Osteoporosis:	Wakabayashi et al Journal of Bone and Mineral Research (2002) 17; 249-256	This paper shows PDE7 mRNA expression in bone osteoblastic cell lines and therefore provides a link between PDE7 and osteoporosis.

Applicants respectfully submit that the literature references provided herewith, together with other literature cited in the application, provide guidance to one of skill of the art for a link between PDE7 inhibitors of the present invention and the claimed diseases/disorders.

As a courtesy to the Examiner, copies of the literature references discussed above are attached hereto.

Accordingly, Applicants submit that the rejection of claims 12-16 (now claims 13-16) under 35 U.S.C. § 112, first paragraph, has been overcome. Applicants respectfully request that the rejection be withdrawn.

Claims 1-17 stand provisionally rejected under the judicially created doctrine of obviousness – type double patenting as allegedly being unpatentable over claims 1 and 3-26 of co-pending application 10/852,404 (or US2004/021483 A1). It is alleged in the Office Action

that the instant formula (I) overlaps with the formula (I) of the co-pending application when variables of the co-pending application have the following meanings:

i. X_1-X_4 are independently $-C(R^1)-$; wherein R^1 is alkyl (which corresponds to the instant R^1) or R^1 is X^5R^5 (which corresponds to the instant $-OR^2$);
ii. Y is NR^{12} wherein R^{12} is hydrogen;
iii. A is a ring of 4-, 5- or 7-membered ring with ring atoms of A^1, and/or A^2, A^4, A^5;
iv. Z is O.

Further, it is alleged that "[c]laim 1 of the co-pending application differs from the instant claim 1 by having a broader scope and reciting formulae II & III. However, regarding Formula I, there is substantial overlapping subject matter as listed above. Further more, two species in claims 22 and 23 of the co-pending applications (see US 2004/214843 A1 page 66 left column, lines 49 and 52; also page 67, right column, lines 10 and 13) read on the instant Formula (I)".

Applicants respectfully submit that there is no overlap between the claims of US 2004/214843 A1 and the claims of the present application for the reason set forth immediately below. First, the claims of US 2004/214843 A1 define that the at the 5'-position (the group X_1) may be X^5R^5 or Q1. The group Q1 may be OR^2.

Further, in the '843 application, the R^5 is restricted to aryl, heteroaryl, cycloalkyl (optionally incorporating C=O or a heteroatom) or cycloalkenyl (optionally incorporating C=O or a heteroatom). These groups are not included in the definition of R^2 in the present application.

In the alternative, the group R^2, in the US 2004/214863 A1 may be a lower alkyl which may be further substituted with, among other things, OR^6, $COOR^6$, NR^6R^7, $NR^6C(=O)R^7$, $C(=O)NR^6R^7$ or $SO_2NR^6R^7$.

In the claims of the presently pending application, the equivalent group R^2 is defined as $(C_1$-$C_6)$alkyl which is further substituted with OR^4, $COOR^4$, NR^4R^5, $NRC(=O)R^4$, $C(=O)NR^4R^5$

or $SO_2NR^4R^5$, and R^4 and R^5 are in turn, $(C_1$-$C_6)$alkyl which is further substituted (in the case of R^4) and may be further substituted (in the case of R^5). Therefore, it can be seen, that the groups R^4 and R^5 in the claims of the presently pending application are equivalent to the groups R^6 and R^7 in US 2004/214863 A1.

However, the substituents on the groups R^4 and R^5 in the claims of the present application are different than those on the groups R^6 and R^7 in US 2004/214863 A1. In US 2004/214863 A1, the groups R^6 and R^7 may be hydrogen or lower alkyl which may be substituted with one to three OR, COOR or $NR^{23}R^{24}$ wherein R, R^{23} and R^{24} may be hydrogen or lower alkyl (or in the case of R, additionally CN or SO_2NH_2). In the claims of the present application, the substituents on the groups R^4 and R^5 do not include OR, COOR or $NR^{23}R^{24}$. Additionally, as a substituent must be present on the group R^4 in the present application, the possibility in the present application of R^4 being unsubstituted alkyl is excluded. There is, therefore, no overlap between these groups in the present application and those of US 2004/214863 A1.

In the alternative, as outlined above, the group R^2 in the present application may be $(C_1$-$C_6)$ alkyl which must be substituted with $OC(=O)R^{4a}$, SR^{4a}, $S(=O)R^3$, $C(=NR^9)R^{4a}$, $C(=NR^9)$-$NR^{4a}R^{5a}$, NR-$C(=NR^9)$-$NR^{4a}R^{5a}$, $NRCOOR^{4a}$, NR-C(=O)-$NR^{4a}R^{5a}$, NR-SO_2-$NR^{4a}R^{5a}$, NR-$C(=NR^9)$-R^{4a} or NR-SO_2-R^3. These substituents are not present in the list of possible substituents for the equivalent group R^2 in the US 2004/214863 A1. Therefore, there is no overlap between these groups in the claims of the present application and those of US 2004/214863 A1.

It is stated in the Office Action that the compound cited on page 66, left column left column, lines 49 and 52 (corresponding to Examples 81 and 82) are within the scope of the present application. Applicants respectfully submit that these compounds fall outside the scope of the present application for the reasons set forth immediately below. First, in Example 81 of US 2004/214863 A1, the group X_1 is C-OCH_2CN. This falls outside the present claims as CN is not included in either list of the substituents on the $(C_1$-$C_6)$ alkyl group immediately attached to the oxygen atom (see the two square bullets).

Secondly, in Example 82, the group X_1 is C-OCH_2-(1H-tetrazol-5-yl). This also falls outside the claims of the present application wherein the group Q^2 is a saturated heterocycle, not a heteroaryl group such as tetrazolyl.

Accordingly, Applicants respectfully submit that the claims 1-17 are patentably distinct from the claims of US 2004/214863 A1 and respectfully request that the rejection of claims 1-17 under the judicially created doctrine of obviousness – type double patenting be removed.

In view of the present amendment and forgoing remarks reconsideration of the rejection and advancement of the case to issue are respect fully requested.

The Commissioner is authorized to charge any fee or credit any over payment in connection with this communication to our Deposit Account No. 23-0455.

Respectfully submitted,

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